EDUCATION FOR NURSES ON THROMBOELASTOGRAPHY TO INFORM ANTICOAGULATION THERAPY IN EXTRACORPOREAL MEMBRANE OXYGENATION

by

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As members of the DNP Project Committee, we certify that we have read the DNP project prepared by *Amy L. Moore*, titled *Education for nurses on thromboelastography to inform anticoagulation therapy in extracorporeal membrane oxygenation* and recommend that it be accepted as fulfilling the DNP project requirement for the Degree of Nursing Practice.

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Final approval and acceptance of this DNP project is contingent upon the candidate's submission of the final copies of the DNP project to the Graduate College.

I hereby certify that I have read this DNP project prepared under my direction and recommend that it be accepted as fulfilling the DNP project requirement.

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TABLE OF CONTENTS

TABLE OF CONTENTS – *Continued*

LIST OF TABLES

ABSTRACT

Extracorporeal Membrane Oxygenation (ECMO) therapy is a growing and developing therapy in critical care medicine for patients that are in severe cardiovascular and/or pulmonary failure. This patient population is very complex, including complex coagulopathies. These coagulopathies are related to both the underlying cause and to the ECMO circuit itself. Current knowledge and available tools are quickly evolving while clinicians and researchers look for better ways to understand and treat this patient population. This rapidly changing care environment has not provided any standardized education for registered nurses (RNs) that are caring for these patients at the bedside. This DNP project attempts to close this gap in knowledge and provide digestible information for RNs to better the care that they provide to the ECMO patients in regard to coagulopathies. An education module based on the most current research and common practices was developed and shared with clinicians with a variety of backgrounds that care for ECMO patients. Their expert opinions were elicited to evaluate and provide the necessary feedback to ensure that the education would achieve closing this gap of knowledge. Finally, this module will be disseminated through publication to share with the critical care community.

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a therapy used in the intensive care units (ICU) as a life support therapy. This therapy provides the support to the lungs, heart, or both organs in critical illnesses, such as acute respiratory distress syndrome (ARDS) or a myocardial infarction (MI). This therapy affords the affected organs time to heal while on other medical supportive therapies to reverse the cause of the insult (American Thoracic Society, 2016). ECMO is invasive as it requires a large catheter(s) that carry large amounts of blood outside of the body through an oxygenator and a pump that replaces oxygen, removes carbon dioxide (CO_2), and pumps the blood back to the body (American Thoracic Society, 2016). The ECMO machine can filter and pump between three to eight liters per minute (American Thoracic Society, 2016). The machine must be closely monitored and managed by a trained nurse, respiratory therapist, or perfusionists, called an ECMO specialist (American Thoracic Society, 2016). This therapy carries high risks of coagulopathy such as thrombosis and bleeding. The risk of thrombosis is treated with anticoagulants, and often, because of this treatment and other inflammatory reactions, bleeding occurs. Current research and common practice supports the use of activated partial thromboplastin time (aPTT) and activated clotting time (ACT) laboratory values to titrate anticoagulants to mitigate these risks (Bollinger, Zenklusen, & Tanaka, 2016). These tests measure very specific fragments of the clotting cascade, and do not provide an overall assessment of the individual patients clotting propensities (Bollinger, Zenklusen, & Tanaka, 2016). Because ECMO increases the complexity of coagulopathies, the suitability of these specific tests in this population may be brought into question (Bollinger, Zenklusen, & Tanaka, 2016).

Thromboelastography (TEG) testing is a laboratory method that provides a comprehensive assessment of complex coagulopathy. It has progressively been utilized in critically complex patients, particularly trauma patients (Da Luz et al., 2014). However, how this laboratory method can improve the management of coagulopathy complications in patients requiring ECMO therapy has yet to be explored in depth.

Background Knowledge

ECMO

Several types of therapeutic application for ECMO are practiced. Venovenous (VV) is used to support hypoxic, hypercapnic, or mixed respiratory failure when mechanical ventilation is unable to support ventilation or as a bridge to lung transplantation (Conrad & Rycus, 2012). VV ECMO uses an oxygenator that acts as an artificial lung, allowing oxygen and carbon dioxide gas exchange (Makdisi & Wang, 2015). It is the fastest growing modality in adults, gaining momentum following the CESAR trial (Peek et al., 2009). Before this study, the use of ECMO in adults was thought to have little benefit based on previous RCT's (Conrad & Rycus, 2012). The development of a dual lumen cannula with percutaneous cannulation around this time also contributed to the safety of VV EMCO in adults (Conrad & Rycus, 2012).

Venoarterial (VA) ECMO is used for cardiac failure that has not responded to other supportive measures, such as fluid resuscitation, inotropic agents, or an intra-aortic balloon-pump (Makdisi & Wang, 2015). This modality is also growing in usage, but survival rates remain consistently low around 44% (Conrad & Rycus, 2012). In VA ECMO, the cannulas are positioned in the vena cava to off load the work of the heart, and subsequently the rest of the heart. This allows time for the contractile function to return. The blood is returned to the aorta in

retrograde direction, which raises blood pressure and allows for end-organ and coronary perfusion (Thiagarajan, Yarlagadda, & Bratton, 2012).

VAV ECMO is also used for patient's that are in multiorgan system failure and require the support of both cardiac flow and respiratory support. This can be managed by adding or changing the insertion sites of the ECMO cannulas. Extracorporeal cardiopulmonary resuscitation (ECPR) is emergency cannulation for ECMO typically performed in the emergency room incorporated into cardiopulmonary resuscitation (CPR) with a percutaneous approach, but the mechanism of the therapy remains the same (Pappalardo & Montisci, 2017). Improved outcomes compared to conventional CPR have not been established and the efficacy is still being debated (Pappalardo & Montisci, 2017). For the purpose of this project, education will focus on VV and VA ECMO.

Patients that are considered for ECMO are among the most critically ill. It is a last resource when other methods of life support have failed. The Murray Score can be used to determine the need of a referral to an ECMO center for respiratory failure when other methods have failed to properly oxygenate the patient. With increasing rates of utilization of ECMO, Extracorporeal Life Support Organization (ELSO) also recommends tools to help predict mortality of adult patients for VA or VV ECMO, including the Survival after Veno-Arterial ECMO (SAVE) score or the Respiratory ECMO Survival Prediction (RESP) score. These scores are based on the ELSO registry where ECMO centers internationally enter their data on patient outcomes and ECMO run details (Schmidt et al., 2014; Schimdt et al., 2015). These scores help clinicians to guide treatment in these critically ill patients based by stratifying risks and predicted

mortality, with the understanding that this tool is not to assess who goes on ECMO (Schmidt et al., 2015).

ECMO and the pro-coagulant state. The use of ECMO as a supportive or rescue therapy for patients in acute severe cardiac failure, and/or severe respiratory failure has been well documented (Auborn et al., 2013). The most common complications related to ECMO are major bleeding, found in about 30% of this population, and thrombosis, found in 15% according to ELSO (Aubron et al., 2013). However, thrombosis is likely underdiagnosed (Aubron et al., 2013). Thrombosis and major clot formation in the circuit can be fatal (Aubron et al., 2016). Because the development of thrombosis presents such a high mortality risk, intravenous anticoagulants are routinely used prophylactically (Aubron et al., 2016). Anticoagulation therapy can be conservative or aggressive depending on the needs of the patient and whether they require VV ECMO or VA ECMO (ELSO, 2014). As a result of anticoagulation therapy, increased bleeding can occur and then is managed by regularly reviewing laboratory values (e.g., aPTT, ACT, TEG) anticoagulation therapy is subsequently adjusted as needed (Aubron et al., 2016).

To understand the complexity of the coagulopathy of an ECMO patient, health professionals need to understand the pathophysiology of these complex complications. There are several events that can increase the risk of thrombosis in this population. The illness the patient is experiencing can cause a systemic inflammatory response syndrome (SIRS) or disseminated intravascular coagulation (DIC), through either trauma, major surgery, massive blood transfusion, or sepsis (Samuels, Moore, & Moore, 2018). This causes activation of the clotting cascade that can result in increased formation of thrombin and subsequently, thrombosis and bleeding in the case of DIC (Samuels, Moore, & Moore, 2018). ECMO exposes the blood to a

non-endothelial artificial surface, which also can trigger an inflammatory response (Esper et al., 2017).

One of the body's inflammatory response to exposure of blood to the ECMO circuit is hypercoagulopathy. In healthy individuals, fibrinolysis is the natural response of the clotting cascade to clot formation and subsequent breakdown in the production of plasmin and plasminogen activators. (Kolev & Longstaff, 2016). Hyperfibrinolysis (sometimes referred to as primary) occurs in a disease state such as liver cirrhosis where many clotting factors produced complicate the balance of such factors (Kolev & Longstaff, 2016). Secondary hyperfibrinolysis becomes a concern in ECMO patients, usually identified as an aspect of disseminated intravascular coagulation (DIC). DIC in ECMO patients is a process that lacks definitive identification in ECMO populations based on the scoring system criteria from the International Society on Thrombosis and Haemostasis (Bembea, 2016). This phenomenon is rare in ECMO but presents one of the more complex challenges in managing coagulation in patients.

ECMO and anticoagulation management. The current use of anticoagulants to prevent thrombosis and manage bleeding requires further explanation to better understand how TEG might improve management in this population. Esper et al. (2017) looked at multiple academic institutions from North America, Europe, Australia, Asia, and South America to examine the differences in anticoagulant methods in their ECMO programs. Most programs used heparin, with only two using bivalirudin (Esper et al., 2017). Many of the programs used aPTT, ACT, or antithrombin III (AT) levels to guide anticoagulant protocols, with many inconsistencies and no agreed upon level of anticoagulation (Esper et al., 2017). About a third use TEG as an adjunct or primary guide to the use of anticoagulants (Esper et al., 2017)

TEG

Thromboelastography is widely used in trauma, hepatobiliary, and cardiac surgeries to identify and predict post-operative bleeding and thrombosis (Hobson et al., 2006). The benefit of this test is that it is a whole blood test that measures a global hemostasis profile, including clotting times (R time), clot kinetics (K, α), clot strength (MA), and clot lysis (LY30) (Lequier, Annich, & Massicotte, 2012). The use of this test has the potential to better assess the needs of the patient on ECMO regarding these issues by looking at a complex and complete method to better target care (Haemonetics, n.d.). Isolated factors of coagulation, such as an ACT or aPTT, are common tests used in titrating anticoagulants in ECMO patients but are isolated factors of the clotting cascade (da Luz, Nascimento, & Rizoli, 2013). By providing a comprehensive depiction of the patient's hemostasis, ECMO may better guide anticoagulation in addition to those isolated values (Hobson et al., 2006).

ECMO as a rescue therapy has only been used and studied in the adult population for about 20 years (Fortenberry, 2012). The utilization of this therapy in adults remains relatively new in the medical world. This is also a population where TEG testing may be ideal for management of the two most common complications- thrombosis and bleeding. Anticoagulation medications, commonly heparin, have been used based on the ease and familiarity of this drug with providers (Lequier, Annich, & Massicotte, 2012). The use of a more comprehensive assessment of the coagulation status holds potential to decrease mortality and complications related to major bleeding or thrombotic complications. TEG also can identify dangerous coagulopathies, such as secondary fibrinolysis, which is otherwise difficult to identify (Kolev &

Longstaff, 2016). Education on better ways to interpret response to therapy is the first step to better outcomes.

Local Problem

In the intensive care units (ICU) at Banner University Medical Center in Phoenix (BUMCP), ECMO is the therapy of choice for severe decline in pulmonary or cardiac function. The ECMO team, including ECMO specialists, the ICU medical team, and the cardiothoracic surgery providers collaborate to manage the anticoagulation therapy for this population. There have been numerous cases of severe bleeding and thrombosed circuits that have resulted in increased complications, longer hospital stays, and high mortality rates. To mitigate these adverse events and better manage these patients, the ECMO team of providers are developing a protocol to titrate bivalirudin and heparin anticoagulation therapy based on both the aPTT and the TEG profile. Because there has been no formal education for nurses and residents regarding TEG and its application to managing an ECMO patient's coagulation state, confusion and uncertainty exist in the team. This uncertainty may impact the success of a new protocol. The development of the protocol and the care of the patients will be better achieved through continuing education of the staff to facilitate best practice and safety for the ECMO patients regarding TEG application and anticoagulation.

Purpose

There is an identified need for more practitioners to understand the benefits of TEG testing in high risk patients of hemorrhage and thrombosis. ECMO patients are an ideal population to examine the benefits to increasing the education and use of TEG in healthcare professionals. The purpose of the proposed project is to develop a continuing education model on

the pathophysiology, interpretation, and practice implications of TEG use in patients on ECMO. The intent is not to make recommendations to anticoagulation protocols, but to better support the principles of ECMO, including the use of TEG, and anticoagulation strategies, to support patients. Further, the continuing education module may be useful for not only local nurses but may serve as a publishable continuing education module that would serve a wider population of nurses. This notion underpins the study question/aims of this project.

For registered nurse ECMO specialists (P), is an educational module on the use of TEG in ECMO patients (I) useful with respect to providing knowledge of pathophysiology, interpretation, and practice applications related to understanding anticoagulation protocols (O)? The aims of this project are to 1) develop a continuing education module on TEG to inform anticoagulation therapies in ECMO; and, 2) solicit expert opinions of ECMO and TEG specialists regarding the usefulness of the continuing education module.

Theoretical Framework

The theoretical framework chosen to guide this project is the Stetler Model. The Stetler Model is a research utilization (RU) framework that provides a guide to incorporate research into evidence-based practice (EBP) (Stetler, 2001). This model is designed to be oriented towards practitioners to guide critical thinking and decision making in both a group setting and for the individual practitioner (Stetler, 2001). This framework encourages and highlights the importance of review and adjustments along the way (Romp & Kiehl, 2009). Stetler (2010) describes research to be developed in three different applications and apply it to this framework: instrumental, conceptual, and symbolic (NCCMT, 2001). Instrumental is the use of objective, factual knowledge, conceptual knowledge changes how a person sees and understands

knowledge, and the symbolic knowledge is the strategic ability to use scientific evidence to persuade or influence policy change or how others use and perceive the knowledge (Stetler, 1994). This project is a continuing education module formatted to improve the knowledge of TEG and its interpretation regarding a patient's coagulable state while on ECMO. By using a theoretical framework to develop an educational module that support decision-making skills, and incorporates different usage of data to persuade change, it facilitates evaluation for individuals and groups, and provides a model for evolving EBP over time (Stetler, 2001).

The phases include preparation, validation, comparative evaluation, application, and evaluation (Romp & Kiehl, 2009). In the preparation phase, a need is identified, variations in practice is evaluated, and an end goal is identified (Stetler, 2010). Regarding this project, there is an identified need for education in understanding the role that TEG can provide in patients with varying coagulable states based on feedback of the ECMO specialists and the ECMO coordinator. Variation in different measures of assessing hypercoagulable states are inconsistent throughout different programs (REF). The second phase, validation, requires the finding, verifying, and investigating the current literature and research available (Stetler, 2010). We discussed the current literature and trends to manage anticoagulants in ECMO patient in the background section. Little research has been published to examine the benefit of TEG in ECMO patients, but it's comprehensive method to examine a comprehensive mapping of the clotting system can better direct care.

Phase three is a comparative evaluation and decision making (Stetler, 2010). For this project, feasibility of the application of this knowledge and its qualifying factors are examined. The need according to the study question is for an improved method of evaluating bleeding and

thrombotic events in ECMO patients. By comparing the practice methods of other institutions in the literature, the decision was made to examine the use of TEG and educating nurses and ECMO specialists in its applicability.

Phase four is where this project becomes actualized. This phase applies instrumental, conceptual, and symbolic knowledge in a formal method of application (Stetler, 2010). Translation of the critiques of the literature and its application to a TEG education module is made to develop and implement a continuing education module to determine if staff are then more comfortable and more likely to utilize the TEG technology in managing anticoagulants in ECMO patients. This application uses multiple strategies to evaluate, such as change agents to provide leadership, interactive education, and follow up education (Stetler, 2010). Passive education is not considered efficient, there needs to be more to influence change (Stetler, 2010). Phase five is evaluation, which can happen at the different types of levels of knowledge described previously (Stetler, 2010). The questions to ask in evaluation of this education module are as follows: Has this educational module changed the conceptual knowledge at the individual level? Has implementation of this knowledge made an instrumental change, by influencing practice or policy for this hospital unit? If successful, can symbolic change be made by disseminating the findings and influencing the practice on a wider arena? The Stetler Model utilizes current research, synthesize of that research in application to an identified need and paves a path to implementation and evaluation all the way through to dissemination of knowledge at the individual level to the global level.

Synthesis of Evidence

The literature is limited regarding utilizing thromboelastography (TEG) in therapies that require long term use, such as in ECMO management. A search was conducted in PubMed, the terms "thromboelastography" and "anticoagulants" were used with 1047 results. By restricting the search down to the last five years and it use in humans, the results narrow down to 205. Excluding literatures focused on ages 19 and older left 133 results. The filter of "ECMO" was added, and four articles were left. The same search terms were used in CINAHL and there were only four results, but each one was specific to an anticoagulant, not in the methods of monitoring patient's response. I then searched "provider education" and "thromboelastography" and there were zero results. Similar searches were conducted with other combinations of these terms. Another limitation to the literature appeared to focus on how the TEG could assess a pathological problem, but not how the use of TEG could inform clinical decision making to avoid complications or guide therapy.

TEG and ECMO have been documented in the literature extensively, however, they have been minimally examined together. Fabbro, Winkler, and Levy (2017) discuss the inability of current literature to show what specific point of care test is most efficient in preventing both bleeding and thrombosis. TEG provides a more comprehensive view than point of care, and therefore could lead the way to changing practice. Instead of looking at the available literature in terms of all the concepts in use together, the concepts were researched on an individual basis.

Extracorporeal Membrane Oxygenation (ECMO)

The literature review confirms that ECMO therapy can increase survival over aggressive ventilatory support. The CESAR trial was a benchmark randomized controlled trial that showed

the efficacy of ECMO in respiratory patients. The authors, Peek et al. (2009), followed patients from 103 hospitals that treated respiratory failure patients and compared the survival rates. Patients in the control group were considered for ECMO if traditional ventilator care was insufficient, yet in both groups, outcomes and survivals rates were higher than expected. There has yet to be a study similar for cardiac failure and ECMO patient to this authors knowledge.

One aspect of ECMO and coagulopathies that is important to evaluate is the circuit. As previously discussed, the inside of the circuit is an artificial surface that can cause an inflammatory response and effect the coagulation profile. Different programs use different machines. Malfertheiner et al. (2016) conducted an observational study to determine if there were different responses for the CardioHelp, Dideco ECC, and the Deltastream systems. Coagulation, inflammatory markers, and hemolysis was found in all the patient, and there was no variance between the different circuits.

Thromboelastography (TEG)

Only one study was found that directly examined the effect and feasibility of using TEG compared to aPTT in managing anticoagulation in ECMO patients. Panigada et al. (2018) found that there were fewer hemorrhagic events, though not significantly, and thrombotic events remained the same. Northrop et al. (2015) took a different method and made their anticoagulation protocol more comprehensive to incorporate multiple individual laboratory values in combination with TEG mapping. Their findings were significant for less bleeding events and longer circuit life. Crochemore et al. (2017) examined altered coagulopathy in critical care patient by comparing TEG whole blood mapping or what they defined as conventional coagulation tests (CCT). CCT include platelet counts, fibrinogen, aPTT, PT, and INR. Patients

were routinely given blood products based on an isolated CCT, but their TEG would show a normal clotting pattern. While there were limitations to the study, they recommend that coagulopathy is better determined using whole blood testing (TEG) versus CCT. Deppe et al. (2016) conducted a meta-analysis comparing TEG and standard laboratory tests in cardiac surgery patient, a population that has high risks for hemorrhagic and thrombotic events. The standard laboratory tests included aPTT, prothrombin, INR, platelet counts, and plasma fibrinogen. Deppe et al. (2016) concluded that bleeding and thrombotic events were significantly decreased when guided by TEG versus the standard laboratory tests, but mortality and hospital stays were not significant. The authors also reiterated the need for more RCT's due to the lack of literature and of higher level of study design. Saini et al. (2016) also examined the disruption in the coagulopathy in children when introduced to an ECMO circuit. Data was examined to see if bleeding events were better predicted when using TEG compared to standard laboratory tests, but they were unable to determine that there was a meaningful difference between the different laboratory monitoring methods.

Anticoagulation Techniques

The literature is very limited on the anticoagulation techniques. Recommended practice includes a bolus dose of heparin intravascularly at the moment of cannulation, including for VV, VA, VAV, and ECPR (Lequier, Annich, & Massicotte, 2012). Sklar et al. (2016) conducted a systematic review to evaluate the different methods that ECMO centers used for venovenous (VV) ECMO. This review is limited to the use of aPTT values as this is what most ECMO centers use and is recommended by ELSO. The aPTT values used by different ECMO centers varied as well. The authors concluded that there is a need for more research to be conducted to

examine the best management of anticoagulation in this patient population. A similar systematic review was done for venoarterial (VA) ECMO management. Sy et al. (2017) compared levels of ACT and aPTT, along with programs that used a multimodal monitoring method including TEG. The results did show fewer adverse effects with a multimodal monitoring method, but it was not statistically significant.

A literature search was conducted to investigate the difference in anticoagulation protocols between VV and VA ECMO. No research was found specifically for ECMO, but much of the current practice is extrapolated from cardiopulmonary bypass (CPB) guidelines developed by the American Society of ExtraCorporeal Technology (AmSECT), Society of Thoracic Surgeons (STS), and The American Society of Cardiovascular Anesthesiologists (SCA) (Shore-Lesserson et al., 2018). The most recent guidelines published recommend the use of heparin and an ACT threshold >480 seconds during CPB based on limited data (Shore-Lesserson et al., 2018). Such high doses can cause bleeding when therapy is extended via ECMO, and there is not a standardized anticoagulation measurement as there is with CBP (Shore-Lesserson et al., 2018). While no literature was found comparing thrombotic events occurring more in VA versus VV ECMO, because of the extensive research of anticoagulation in CBP, which is more closely related to VA ECMO in terms of circulatory rejection and more cannulas for retrograde flow, it can be speculated that risk of thrombi in VA ECMO would be more common.

METHODS

The proposed project is based on the understanding that the integration of new technology and practices in an already dynamic and high intensity program may be confusing or overwhelming for the staff. At the hospital in which the project took place, the ECMO program

has relied on isolated laboratory results, such as an aPTT or ACT, to follow anticoagulation protocols since the program was established in 2011. With the recognition of the TEG process and the sophistication it can provide to the ECMO program, a new protocol is currently being developed, integrating aPTT and TEG results. The nurses need improved education to better implement these developing protocols. Therefore, the aims of this project are to 1) develop an education module on TEG to inform anticoagulation therapies in ECMO; and, 2) solicit opinions of ECMO specialists regarding the usefulness of the continuing education module. The module will then be edited and disseminated to ECMO specialists at BUMCP, as we as prepared for publication.

Study Design

This is a descriptive quality improvement project whose overall aim is to improve nursing knowledge regarding the use of TEG in ECMO patients through the development of an education module using a continuing education format. Feedback from a group of expert and intermediate experience in ECMO and TEG reviewed and discussed their perspectives regarding the usefulness of the continuing education module. The participants' feedback was conclusive that the module would be helpful for current and future ECMO specialists.

Setting

This project took place at Banner University Medical Center (BUMCP) in Phoenix, AZ. BUMCP is the largest hospital in the state of Arizona with 733 beds and is a top teaching hospital. ECMO patients at BUMCP are typically admitted to either the medical-surgical (MSICU) or cardiovascular intensive care units (CVICU). The ECMO program has been in place in this facility since 2011. Recently, the ECMO program awarded the Extracorporeal Life

Support Organization (ELSO) Award for Excellence in Life Support – Center of Excellence Gold level. The number of patients placed on ECMO has fluctuated as the program has grown. In 2017, there were 39 ECMO patients cannulated. As of July of 2018, they surpassed that statistic.

Population

Purposeful and targeted sampling was used to recruit seven participants for Aim 2. First, the ECMO program coordinator, two intensivist physicians who manage ECMO patients, and a representative of the TEG company that supports the hospital's use and education of the TEG equipment were invited in targeted sampling. Next, all ECMO specialists were asked to participate in this project. There are approximately 70 ECMO specialist at BUMCP, all of whom are ICU registered nurses. ECMO specialists are a subset of the ICU staff chosen from the more experienced and skilled ICU RNs. From the volunteers, three RNs were selected from those with who are familiar with working with TEG in the ECMO population. The final expert panel was hoped to have a minimum of five to six members, and seven participated. These participants are experts in their positions and familiar with the use of ECMO, TEG, and anticoagulation strategies. The participants were able to read and speak English.

Recruitment

Recruitment consisted of an informational flyer that were placed in the break rooms of the MSICU and the CVICU, email sent from the ECMO coordinator to the ECMO team and posted in the groups private social media group that communicates information to the team (Appendix B). From the group of volunteers, there were five ECMO specialist participants that volunteered, three of which returned the feedback form. As noted above and in addition, the PI

personally asked the ECMO program coordinator, two intensivist physicians that manage ECMO patients, and a representative of the TEG company to participate in the project.

Data Collection

Aim 1

An education module based on a continuing education (CE) model (~1 contact hour) on the use of TEG to inform anticoagulation therapies during ECMO. To ensure initial content validity, the educational module was developed by the PI, the PI's advisor, Dr. Leslie Ritter, and content expert on the ECMO team.

Because one desired outcome of this study is to publish the educational module as a CE, the module was written to adhere to a professional nursing journal continuing education format. Specifically, the CE format used in *American Nurse Today*, a publication of the American Nurse Association, was followed (e.g., https://www.americannursetoday.com/wp-content/uploads/2015/10/Author-Instructions-2015-16.pdf; https://www.nurse.com/ce-writer-s-guidelines).

The data for Aim 1 is the educational module, however a brief description is provided here. The goal of the module is to improve the understanding of the application of TEG in complex ECMO patients for the ECMO specialist. The objectives of the educational module are to: 1) identify what the different values in a TEG tracing mean in relation to coagulopathy; 2) understand the role of TEG in addition to conventional laboratory values regarding anticoagulation therapy in ECMO patients; and, 3) identify interventions and anticoagulation strategies to treat coagulopathies as interpreted by TEG tracing in ECMO.

In accordance with the *American Nurse Today* format, the educational module includes a brief introduction followed by content on coagulation physiology, pathophysiology, common anticoagulation tests and therapies, and principles of TEG and its application in ECMO patients (~3,500 words). Figures and tables are used to augment the narrative as appropriate. A multiple-choice post-test with review and rationale will follow this content. References and links to additional online resources are included. In accordance with the *American Nurse Today*, the final format is in a word (pdf) document.

Aim 2

After UA IRB approval and prior to initiation of the study, a flyer was posted for members of the ECMO team members in cooperation with the ECMO coordinator that describes the purpose and the process of the study. All participants for the focus panel were voluntary. The PI personally contacted the ECMO coordinator, two intensivist physicians that manage ECMO patients, and a representative of the TEG company. Once the participants (expert focus panel) were selected, the education module was given or emailed to each participant. The educational module (developed in Aim 1) was reviewed by the participants and returned to the PI with edits and feedback provided from a questionnaire sent with the module. The review of the module took approximately one hour of their time (one contact hour).

As mentioned above, the expert group reviewed the module and provided feedback via direct meeting with the PI or returning feedback per review questions (Appendix C). The goal of the expert group was to determine the usability of the educational module. A total of two hours of time (one hour to review materials, one hour in a meeting with the PI), were required of participants in Aim 2.

Data Analysis

For Aim 1, the data is in the form of the educational module itself. For Aim 2, the expert panel reviewed the educational module before a scheduled meeting or returning individual feedback per a provided form (Appendix C). This form had open ended questions focused on the strength and weaknesses identified in the information included in the educational module. The PI and chair analyzed the critiqued and categorized themes and then described changes to improve the content and in preparation for publication.

Ethical Considerations

When conducting research and quality improvement projects, ethical principles need to be reinforced. Respect for persons, beneficence, and justice are addressed to protect and minimize risk to any involved.

Respect for Persons

For Aim 1, a case study was fabricated based on possible real events to present a real patient scenario and avoid using any real patient information. For Aim 2, to avoid coercion, participants (ECMO specialists) were notified of the project by public flyer in the unit and posted in the private social media group page. Agreement to attend the review session was considered acknowledgment of their willingness to participate in the study. Names were not to be included in any data collection, including comments made in open ended questions.

Beneficence

There are no risks to the collection of this data identified. At the end of the study, the CE module will be available for all ECMO specialists at BUMPC.

Justice

The recruitment consists of the whole ECMO team with the oversight of the BUMCP ECMO program coordinator. There were not any conflicts of justice appreciated. This project was aimed at provider practice and does not utilize health disparities based on any potential targeted population.

RESULTS

After an email was sent out and flyers were posted, there were nine volunteers. Due to the difficulty or inability for the volunteers to be available for one group, the education module and questions in the script were emailed or provided as a hard copy of the module to the participants they were not able to attend a live focus group session. UA IRB approved this change in data collection (Appendix E). In total, seven participants reviewed the education module and provided feedback. Of those, one meeting was held with the PI and two participants, and five participants reviewed the module on their own and feedback was submitted by email using the questions scripted for the originally planned meeting.

The participants included the ECMO coordinator and educator (RN) of the ECMO team, a hemostasis and TEG clinical consultant (RN) from Haemonetics Corporation, two critical care intensivist physicians, one RN ECMO specialist with four or more years of experience on the ECMO team, and two RN ECMO specialists with two years of experience. Below is a table with their responses (Table 1).

TABLE 1. *Focus expert opinions.*

Question	**Intensivist**	**Intensivist**	**TEG Representative**	**ECMO Coordinator**	**ECMO Specialist**	**ECMO Specialist**	**ECMO Specialist**
Comfort with interpreting TEG	Expert	Expert	Expert	Expert	Intermediate	Intermediate	Novice
Vignette presents a common patient situation	Yes, good scenario to make you think	Yes	Very Well	Excellent	Yes, painted a clear picture	Very well	Yes, good representation
Does the module address anticoagulation in ECMO?	Partially, anticoagulation in an ECMO patient is much more complicated than can be summed up here	Partially, anticoagulant needs with VA patients are relatively increased, would need discussion on circuit set up	Yes	Yes	Yes, it addressed anticoagulation needs	Yes, needs clearly explained, reinforced with posttest questions	Yes, shows the benefit of TEG as another tool to understand a complex situation
Does the module improve knowledge of how TEG works?	Yes, it was clear	Case examples with interpretations would improve the quality of the instruction.	Yes, with small edits	Yes	By simplifying each value and then looking at the TEG as a while, it provided an easy, digestible explanation	Yes, the elements of the TEG are revealed and how it is applied to the patients.	Shows how the TEG is applied and why physicians ask certain questions in relation to the patient's condition
How well does it tie ECMO and TEG together?	Ties it together well	Clarify that TEG does not provide more information because of coagulopathy, coagulopathy is already skewed in an ECMO patient	Very well	Very well	Ties ECMO and TEG together well, breaks it down. Appreciate discussing the basics of ECMO and the necessity of anticoagulation	Very well, connection to what the ECMO specialist will see at the bedside is especially important	Ties together TEG and ECMO very well

TABLE 1 – *Continued*

Question	**Intensivist**	**Intensivist**	**TEG Representative**	**ECMO Coordinator**	**ECMO Specialist**	**ECMO Specialist**	**ECMO Specialist**
Areas of confusion?	DIC diagnosis versus coagulopathy, DIC is a coagulopathy	Clarify areas of interchangeable phrases of hypercoagulopathy and hypercoagulability	K value and α-angle clarification of information, the use of MA_{AA} in platelet mapping	Clarify TEG and TEG with heparinase in vignette and in post test questions	No	No	No
Missing Information?	Clarify that these concepts are new and evolving	No	Add reference to ELSO's "Red Book"	No	No	No	Comprehensive
Additional suggestions	Case studies with TEG pictures	Minor grammatical errors. Different picture example of skewed TEG waveforms	No	No	Add step by step interpretation examples	No	No

TABLE 2. *Feedback themes.*

Recommendations	• Clarify that the technology and understanding of the interaction with blood and the circuit is still evolving. • DIC is a type of coagulopathy, may be confusing to differentiate them • Correct information on K value, α-angle, and platelet mapping • Adding a detailed case study and step by step interpretations of a real TEG • Reference to addition of TEG use in ELSO recommendations
Done well	• Vignette provided a clear picture of a common situation in an ECMO patient with coagulopathy issues identified by TEG • Clear description in how TEG can benefit and be used to assess coagulopathy and effectiveness of anticoagulants in ECMO • Clear descriptions of the individual values in a TEG

Content themes that came up multiple times in the participant feedback was to better clarify that the technology involved in treating and evaluating this patient population is a moving target, and research has not established gold standards or specific guidelines on how to manage anticoagulation in this patient population. As there is still difficulty conducting randomized control studies given the acuity of this patient population, literature is lacking on best practice, but is evolving. The Extracorporeal Life Support Organizations (ELSO) publishes a "Red Book" of recommendations that are updated approximately every five years. This is the first year that it has included recommendations on the use of TEG in ECMO patients. It was also recommended that this information be included in the education. Detailed case studies and visual examples of the step by step interpretation of a real TEG was also suggested.

Positive feedback was also included in the reviews. The vignette was regarded as a good example of a common ECMO patient with an underlying coagulopathy that would otherwise not have been identified with single value laboratory values (i.e., aPTT or ACT). A table was included as a quick reference point for normal ranges of values and possible intervention for abnormal results. Descriptions of each value was also made in greater detail and was also found to be helpful in understanding the content.

DISCUSSION

ECMO is a quickly evolving therapy which is gaining a lot of attention in recent years. ECMO can be associated with severe bleeding disorders and healthcare providers may be challenged to understand new assays to assess coagulation, such as thromboelastography (TEG). Recognizing the gap in knowledge and identifying the needed education on the use of TEG are the first steps in providing optimal care for ECMO patients. The overall purpose of this project was to provide education for the ECMO specialist. First, based on current literature, the PI developed a continuing education module. The education module was then validated by soliciting expert opinions from a diverse group of practitioners (study participants) that work closely with the ECMO population. The education module below includes many of the recommendations of the expert practitioners. In being consistent with the feedback, it was noted that this patient population is complex, and the education provided is to provide a framework for practice, as the decisions made in treating these patients with anticoagulation should be based on assessment of the individual patient and the provider's clinical judgement. Being mindful of publisher's expectations for continuing education modules (American Nurse Today, 2016; Nurse.com, n.d.), the content changes that were made to the CE module that was initially developed were largely based on the input from the TEG representative and were made to clarify the information. These changes included clarification of the k value and α-angle and platelet mapping. The CE module (Appendix E) contains the following criteria as required by the publisher (American Nurse Today, 2016; Nurse.com, n.d.): Abstract of approximately 150-200 words, one sentence goal statement, core competencies, three objectives, a clinical vignette,

introduction, an original, researched, referenced manual of 3,600 words, complete reference list, and a 12 multiple-choice question post-test with the correct answers indicated.

DNP Essentials

This DNP project was written, developed, and implemented in compliance with the University of Arizona's DNP essential elements. For Essential I, scientific underpinnings for practice, this project used research from biophysical, analytical, and organizational sciences through development of education that pulls information and practice from multiple organizations, including BUMCP, Haemonetics, and protocols from published literature from ECMO centers internationally. Complex pathophysiology of the hematological and circulatory systems is discussed in detail, along with applied critical care thinking.

For Essential II, organizational and systems leadership for quality improvement and systems thinking, this project achieves this through developing education that is not available in a comprehensive manner for clinicians on a complex patient population in effort to better the care provided to them. The education was also written with the intention to also be able to be beneficial to clinicians outside of BUMCP with room for adjustment as each hospital or ECMO center differs in their specific anticoagulation protocols. Also, task force of members from multiple disciplines was organized and lead in developing and evaluating the education module.

Essential III, disseminate findings from evidence-based practice and research to improve healthcare outcomes, is met through incorporating this education into the BUMCP ECMO education program. This education module was also written with the intention of publication, in the form of a continuing education module per ANA and CE Direct guidelines, to disseminate it to other hospitals and ECMO centers.

This project also meets criteria for DNP Essentials VI, interprofessional collaboration for improving patient and population health outcomes. This project relied on the collaboration between physicians, nurses, and consultants to develop a cohesive product that has not been otherwise developed. It pulls data and practice guidelines from different peer reviewed policies and practices, both from BUMCP and other published works to provide clear education on management of a complex patient population and new application of TEG technology.

The last of the DNP essentials met in the development of this project is Essential VIII, advanced practice. By creating education for nurses to support their practice and communication with providers, this project also creates a framework for future education to grow as the technology and application of different tools to evaluation coagulopathy and anticoagulation in the ECMO population changes. By designing, developing, and implementing a process of evaluation for the education, this project also conducted a comprehensive evaluation of the material to support best practice regarding the recommendations for the care of this special population.

Conclusion

The ECMO patient has many complexities in the management of their care, not the least of which involves a coagulopathic state. While researchers and clinicians are actively working to develop better ways to monitor and treat the coagulopathy associated with the ECMO patient, there is little standardized education available about monitoring anticoagulation for the bedside RN ECMO specialists. This DNP project attempts to address this gap in education and support the advancement of the RN in furthering their ability to care for this population. By developing a continuing education module on the use of TEG in ECMO patients and eliciting the opinions of

experts, this project hopes to close this gap in knowledge and disseminate the continuing education module to the broader healthcare and critical care community via its publication in a peer review journal. Ultimately, it is hoped that this CE module will result in optimal care of the ECMO patient.

APPENDIX A:

EVIDENCE APPRAISAL TABLE

Reference	Research Question/Hypothesis	Study Design	Sample and Setting	Methods for Data Collection and Data Analysis	Findings
Crochemore, T., Correa, T. D., Lance, M. D., Solomon, C., Neto, A. S., de Campos Guerra, J. C., … & Silva, E. (2017).	Can TEG better detect coagulation disorders than conventional coagulation tests (CCT) and prevent unnecessary blood component transfusions?	Retrospective observation study	**Sample:** 531 patients, every patient that was admitted to the ICU between September 1, 2012 to September 30, 2014. **Setting:** Hospital Israelita Albert Einstein, ICU, Sao Paulo, Brazil	**Data Collection:** Chart review retrieved demographic data, cause of admission, comorbidities, length of stay, mortality, TEG and CCT results during stay (includes platelet counts, fibrinogen, aPTT, PT, and INR). **Data Analysis:** Descriptive statistics were compared, variables evaluated by the Kolmogorov-Smirnov test, group comparisons were made regarding CCT and TEG results using chi-square or Fisher's exact test, and continuous variables were examined using ANOVA and Tukey test.	Coagulopathy when defined by CCT showed more patients were at higher risks for bleeding and often received blood products to correct specific CCT values. These same patients however, most of them had a normal coagulation profile according to the ROTEG results. Despite limitations to the study, as whether these patients received anticoagulants was unavailable, they recommend that ROTEG has the potential to better predict coagulopathy than isolated CCT.
Deppe, A. C., Weber, C., Zimmermann, J., Kuhn, E. W., Slottosch, I., Liakopoulos, O. J., … & Wahlers, T. (2016).	Discuss current evidence in POCT-guided protocols in severe bleeding after cardiac surgery.	Meta-Analysis	**Sample:** 9 RCT's and 8 observational studies were found with a total of 8,332 post cardiac surgical patients from 1966 to 2014. **Setting:** N/A	**Data Collection:** Date search through Medline, EMBASE, and The Cochrane Library. **Data Analysis:** Primary outcomes analyzed for mortality, bleeding, transfusion requirements, AKI, CVA, and thrombotic events.	This meta-analysis supports the hypothesis that an algorithm of treatment with TEG instead of other conventional laboratory values reduced the amount of bleeding, but not the clinical events. TEG directed therapy can better manage blood transfusions, hemostatic drugs, and coagulation factor concentrates.
Esper, S. A., Welsby, I. J., Subramaniam, K., Wallisch, W. J., Levy, J. H., Waters, J. H., … & Schears, G. J. (2017).	Do ECMO institutions use similar management of anticoagulant and transfusions in adult ECMO internationally.	Survey	**Sample:** N=47 chosen out of 54 (36 from North America, 10 from Europe, 4 from Asia, 3 from Australia, and 1 from South America). **Setting:** Adult ECMO institutions	**Data Collection:** Survey request via Survey Monkey software. Descriptive, self-reporting, and cross-sectional. **Data Analysis:** Types of anticoagulation were compared, heparin vs bivalirudin, coagulation values compared, TEG vs aPTT vs ACT vs ATIII, and the goal ranges for each. Comparison of blood transfusion protocols was conducted regards fibrinogen levels, platelets,	Data disproved the hypothesis that most institutions would follow similar protocols. Large variations in practice were found in the surveyed institutions. A lack of evidence-based guidelines and RCT's are contributed to these discrepancies.

Reference	Research Question/Hypothesis	Study Design	Sample and Setting	Methods for Data Collection and Data Analysis	Findings
				and RBC counts.	
Malfertheiner, M. V., Philipp, A., Lubnow, M., Zeman, F., Enger, T. B., Bein, T., … & Lehle, K. (2016).	Monitor hemostatic changes on ECMO with different ECMO machines.	Observational	**Sample:** Three groups of 18 patients were randomly assigned to three different ECMO machines (N=54): CardioHelp, Dideco ECC.05, and the Deltastream system. **Setting:** University Hospital, Regensburg, Germany	**Data Collection:** Each patient had blood samples taken before ECMO initiation, daily for the first 5 days on ECMO, and 1 day after discontinuing the therapy. Labs drawn were CBC, free hemoglobin, LDH, creatinine kinase, creatinine, aspartate aminotransferase, Quick test (like the INR), aPTT, D-dimer, fibrinogen, antithrombin, C-reactive protein, and interleukin (IL)-6 and IL-8. **Data Analysis:** Laboratory values were compared between the three groups, and changes in values tracked throughout the ECMO run for changes.	The main goal of the study was to examine whether the different machines would influence the hemostasis of the patient's receiving ECMO. While the study did not show any significant changes, the secondary goal of the study was to monitor the changes in the blood in response to the initiation and discontinuation of the therapy. There were significant marker changes in coagulation, hemolysis, and inflammation once introduced to ECMO. Coagulation and hemolysis markers stabilized once ECMO was discontinued, however inflammatory markers stayed the same.
Northrop, M. S., Sidonio, R. F., Phillips, S. E., Smith, A. H., Daphne, H. C., Pietsch, J. B., & Bridges, B. C. (2015).	Do comprehensive ECMO anticoagulation monitoring protocols result in fewer complications?	Retrospective chart review	**Sample:** N=261 CMO runs before the initiation of a protocol, and 105 ECMO runs after the initiation of an anticoagulation protocol. **Setting:** Monroe Carell Jr Children's Hospital at Vanderbilt	**Data Collection:** Complications during ECMO runs were compared before implementing a revised anticoagulant protocol to now include anti-factor Xa assay, antithrombin levels, and TEG to standard ACT, platelet count, protime, INR, aPTT, and HCT. **Data Analysis:** Correlational statistics were compared before and after the implementation of an anticoagulant protocol.	Mean use of blood products were decreased significantly after initiating the new protocol. Bleeding at the cannula site was significantly decreased (p=0.04) and at the surgical incision (p=0.02). ECMO circuit life was also increased (p=0.02). Association of following the protocol confirmed the hypothesis of fewer complications.
Panigada, M., Iapichino, G. E., Brioni, M., Panarello, G., Protti, A., Grasselli, G., … &	Assess the safety and feasibility of anticoagulation protocols in ECMO utilizing TEG versus aPTT	RCT	**Sample:** N=42, all patients were on VV ECMO, from either ARDS or a bridge to lung transplant, over the age of 18, and were not thrombocytopenic (platelet	**Data Collection:** 21 patients were randomly placed on the control protocol (aPTT), and 21 placed on the study protocol (TEG). Baseline aPTT and TEG were done in all 42 patients every morning and then	Safety outcomes: fewer patients had bleeding events in the study group (not significant, p=0.21). Severity of bleeding was not different. Thrombotic events and transfusion rates were similar.

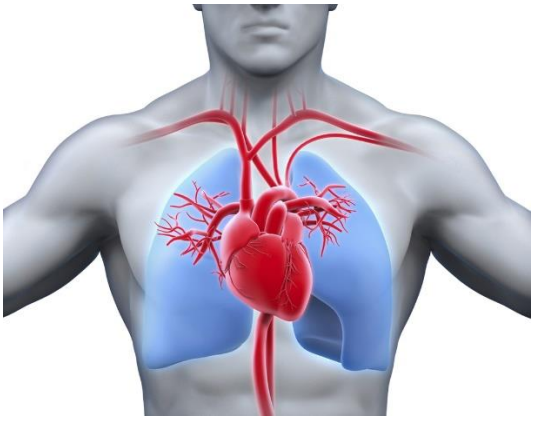
Reference	Research Question/Hypothesis	Study Design	Sample and Setting	Methods for Data Collection and Data Analysis	Findings
Pesenti, A. (2018).			count <30,000/mm^3), and were not diagnosed with HIT **Setting:** Two Italian ECMO referral hospitals in Milan and Palermo.	adjusted according to the assigned protocol based on an R time of 16-24 in the TEG group and an aPTT ratio of 1.5-2 in the control group. **Data Analysis:** Safety was assessed by the amount of hemorrhagic or thrombotic events and required blood transfusions. Feasibility was assessed by how many dose adjustments were needed, number of results within targeted range, and "violations" of protocols, interruptions regarding patient safety or delays in lab results.	Feasibility outcomes: The study group required more rate changes per the protocols (p=0.01). Lab results were more frequently in the targeted range for the control group versus the study group (p<0.001).
Peek, G. J., Mugford, M., Tiruvoipati, R., Wilson, A., Allen, E., Thalanany, M. M., … & Elbourne, D. (2009).	ECMO will increase the survival without severe disability by 6 months compared to traditional ventilatory support.	RCT	**Sample:** 103 Hospitals, including the main ECMO center at Glenfield Hospital, 92 conventional treatment centers and 11 referral hospitals. Patients were intubated, ages 18-65, Murray score of >3.0, uncompensated hypercapnia with pH<7.20 despite treatment. N=180 **Setting:** Glenfield Hospital, Leicester, United Kingdom	**Data Collection:** Patients were randomly placed in either group. Those that received ECMO were transported to Glenfield Hospital. Those that received conventional ventilator support were advised to use a low-pressure and low-volume strategy. Death or severe disability was then tracked six months post treatment to assess quality of life, respiratory symptoms, cognitive psychological state, and lung function. **Data Analysis:** Treatment groups were compared statistically	Only a fifth of patients screened tolerated conventional treatment, and four fifths of the patients needed to ECMO treatment. Survival to six months was greater in the ECMO group. While patients that received conventional treatment had better outcomes than hypothesized, the ECMO group had better outcomes.
Saini, A., Hartman, M. E., Gage, B. F., Said, A., Gazit, A. Z., & Eghyesady, P. (2016).	Assess the incidence of platelet dysfunction via TEG with children on ECMO.	Retrospective chart review	**Sample:** All patients <18 years of age placed on ECMO that had TEG platelet mapping performed during their run. **Setting:** St. Louis Children's Hospital neonatal ICU, cardiac ICU, and pediatric ICU between 9/2011 to	**Data Collection:** Demographics, duration of ECMO run, hemostasis data (ACT, prothrombin, aPTT, platelet counts, fibrinogen, antithrombin activity, TEG platelet mapping, blood products transfused, heparin dose, and other medications that can affect platelet activity. **Data Analysis:** Statistical analysis	Severe bleeding events related to platelet dysfunction occur often in patients on ECMO. The study was not able to predict bleeding events by using TEG platelets mapping due to the size of the study.

Reference	Research Question/Hypothesis	Study Design	Sample and Setting	Methods for Data Collection and Data Analysis	Findings
			12/2012.	examined the qualitative platelet dysfunction by determining frequency of ADP- or AA-mediated platelet dysfunction.	
Sklar, M. C., Sy, E., Lequier, L., Fan, E., & Kanji, H. D. (2016).	Evaluate anticoagulation techniques in VV ECMO patients	Systematic Review	**Sample:** Articles were analyzed from 1977 to 2015 to examine major bleeding events, thrombotic events, and in-hospital mortality. **Setting:** N/A	**Data Collection:** 18 studies were analyzed (N=646) **Data Analysis:** Studies were compared among those that targeted a specific aPTT range, those with aPTT >60 seconds, and targeted aPTT <60 seconds	The published literature is very limited on scope and consistency. This systematic review supports the concept that there is a need for more research and RCT's on the methods of anticoagulants in VV ECMO.
Sy, E., Sklar, M. C., Lequier, L., Fan, E., & Kanji, H. D. (2017).	Compare anticoagulation practices and prevalence of bleeding and thrombotic events in VA ECMO.	Systematic review and meta-analysis	**Sample:** 26 studies with n=1496 patients were analyzed from 1977 to September 27, 2016. **Setting:** N/A	**Data Collection:** Search of multiple electronic databases including Medline, PubMed, PubMed Central, EMBASE, Current Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials. **Data Analysis:** Descriptive statistics were used to analyze frequencies of major bleeding, thrombotic events and estimates of mortality rate based on the type of multimodal methods of monitoring anticoagulants.	Bleeding events occurred in 13% of the patients when lower ACT (180 seconds) was used, compared to 28% with those using ACT >180 seconds, 50% in patients monitored with aPTT, and 24% of patients using mixed methods. Thrombotic events occurred in 12% in patient monitored with ACT<180 seconds, 9% in patients monitored with ACT >180 seconds, 3% of patients monitored with aPTT, and 6% in patients with mixed monitoring methods. The authors conclusion is that there is not enough data to support one method over another and further investigation is warranted.

APPENDIX B:

RECRUITMENT FLYER

ECMO TEAM



Needed: team members that are well versed in TEG interpretation to review a continuing education module for the new and future ECMO specialist
Your opinions will also be included in my doctoral project (no names)

If you would like to be part of this exciting education opportunity, please responds/contact me at
Amy.Moore@bannerhealth.com

Requirements:
Read the CE (1 hour)
Meeting with me and others to discuss your feedback (about 2 hours)
Maybe learn something new

APPENDIX C:

RECRUITMENT EMAIL FROM ECMO COORDINATOR

ECMO team members,

You are invited to participate as a volunteer to give feedback on one of our team member's doctoral project. Amy Moore has been working on developing a continuing education module to help better inform our team members and future members on how we are applying TEG results in helping inform the anticoagulation management of our patients. If you are interested, she will email you the module in advance and then will schedule a meeting with 5-6 TEG experts to evaluate the effectiveness of the module and gather any additional feedback you have. It will take about an hour to read, and she asks that you be willing to participate in a meeting for about 2 hours. Please let me know who would be interested in helping to contribute to this educational opportunity.

Thank you,

Stacy Gerle, RN

BUMCP ECMO Coordinator and Educator

APPENDIX D:

FOCUS GROUP SCRIPT

Focus Group Questions

1. How comfortable are you with interpreting TEG's with the ECMO patients?
2. How well did you think the vignette in CE module served as an example to how TEG can alter treatment in ECMO patients?
3. Did the module address anticoagulation needs in ECMO?
4. How did the TEG information improve knowledge of how TEG's work?
5. How well does the education tie ECMO and TEG interpretation together?
6. Are there areas that are unclear or confusing?
7. Was there any information that was lacking or missing?
8. Is there anything else anyone would like to add or suggest?

APPENDIX E:

ECMO CONTINUING EDUCATION MODULE

Thromboelastography (TEG) and Its Role in Interpreting Anticoagulation in Extracorporeal Membrane Oxygenation (ECMO)

Goal: The goal of this module is to improve the understanding of the application of TEG in a complex ECMO patient for ECMO specialist.

Core Competencies:

1. Better practices regarding the care of ECMO patients.
2. Understanding the role of the nurse in managing anticoagulation in the ECMO patient.
3. Improving communication between nursing and physicians.

Objectives:

1. Identify what the different values in a TEG tracing mean in relation to coagulopathy.
2. Understand the role of TEG in addition to conventional laboratory tests regarding anticoagulation therapy in ECMO patients.
3. Identify interventions to treat coagulopathies as diagnosed by interpreting by TEG tracings.

Clinical Vignette

Mrs. Day has been on venovenous (VV) ECMO for 2 days from pneumonia that had progressed to severe acute respiratory distress syndrome (ARDS). Her blood pressure has been decreasing, she has a low-grade fever requiring you to cool the circuit, and she is requiring more vasopressor support. There is increased bleeding at the cannula site and dressing changes are needed every few hours. She is on a heparin drip titrated to aPTT between 65-80 seconds and has blood drawn for TEG analysis every 12 hours. Her most recent lactic acid is 5.2 mmol/L, up from 1.8 mmol/L yesterday. This morning her TEG with heparinase values were: R time 4.5 seconds, MA75 mm, and LY30 32%. The most recent aPTT is 75. Standard TEG values were: R time 12, MA 80 mm, and LY30 28%.

Question 1- Which of the above out of range value is concerning?

A. R
B. MA
C. LY30
D. All of the above

Question 2- What disease process do you suspect?

A. Cardiogenic shock
B. Sepsis
C. Hypercarbic respiratory failure
D. ECMO circuit failure

Question 3- What coagulopathy do you suspect is occurring?

A. Nothing, this is normal
B. Secondary fibrinolysis
C. Hypercoagulable

D. Primary fibrinolysis

Question 4- What are the proper interventions for the diagnosis you made in Question 3?

A. Notify the provider for change in laboratory values
B. Increase the rate of the heparin per your hospital protocol
C. Hold the heparin and prepare for possible blood transfusion
D. Continue the current plan of care

Abstract

Coagulopathy occurs when the blood's ability to control clotting is impaired. Coagulopathy is complex, and in ECMO patients, it becomes even more so. Conventional laboratory tests such as an activated partial thromboplastin time (aPTT) and activated clotting time (ACT), can identify pieces of the coagulopathy puzzle but may not reflect the more complex pathophysiology. With the addition of TEG analysis, the ECMO specialist can better understand the ECMO patients' coagulopathy, anticipate complications, and communicate with providers regarding the best plan of care. This CE will help the ECMO specialist understand what a normal TEG tracing is, what abnormal values to look out for, and how those values pertain to their patient.

Introduction: Background and Current Research

ECMO has two different applications in critically ill patients. Venovenous (VV) is for pulmonary support in severe lung failure, while venoarterial (VA) is cardiac support for severe cardiac failure. ECMO therapy is associated with coagulopathies such as thrombosis and bleeding. These disorders can be related to the primary diagnosis itself, as well as from exposure the large amount of foreign surface of the ECMO circuit. Because the inner lining of the ECMO circuit does not mimic the endothelial lining of the patient's vasculature, platelet activation and adherence to the circuit and activation of clotting factors can occur. The sum of these processes leads to a widespread inflammatory response which interferes with the body's ability to properly manage its own coagulation factors and, if left untreated, thrombosis can occur. To prevent thrombosis, ECMO patients are treated with anticoagulants. Paradoxically, because of complex interactions among inflammatory processes and anticoagulant treatment of inflammatory reactions, abnormal bleeding can also occur in these patients. Understanding coagulopathy in the ECMO is evolving and those in the medical community are still trying to better understand the interaction with the circuit, as well as the tools available to assess it.

Current research and common practice support the use of activated partial thromboplastin time aPTT and activated clotting time (ACT) testing to titrate anticoagulants to prevent thrombosis and mitigate bleeding (Bollinger, Zenklusen, & Tanaka, 2016). APTT is a blood test that measures clotting factors in the intrinsic system, including XII, XI, VIII, and IX. ACT is used while patients are receiving unfractionated heparin, also measuring the factors of the intrinsic clotting system, to the start time of clot formation. These two tests measure the time to clot formation and are useful in monitoring anticoagulation, but do not provide a comprehensive assessment of the individual patients' coagulation profile (Bollinger, Zenklusen, & Tanaka,

2016). Because ECMO increases the complexity of coagulopathies, the use of additional tests such as TEG may be warranted (Bollinger, Zenklusen, & Tanaka, 2016).

Thromboelastography

TEG is a whole blood viscoelastic blood assay test that measures the lifespan of a clot. It is not a substitute for aPTT or ACT but provides additional information of the coagulopathy of an ECMO patient, such as information about platelet activity, coagulation, and enzymatic pathways. TEG technology was first introduced in 1948 but has gained more popularity in the recent decades as computer technology has advanced its ease of use (Whitten & Greilich, 2001). TEG is commonly used in trauma, cardiac and liver surgical cases. To date, TEG has not been extensively examined in the ECMO patient. Several studies have indicated that when used in conjunction with aPTT and other isolated coagulation tests, fewer significant bleeding and thrombotic events occur (Panigada et al., 2018). These studies provide evidence that the use of TEG could potentially benefit ECMO patients and as its use in this population increases, ECMO specialists will require specific knowledge of TEG testing. The Extracorporeal Life Support Organization (ELSO) has recently added recommendations for the use of TEG in ECMO to their "Red Book", which is a benchmark reference for ECMO programs internationally. This guideline reference is updated along with the latest advances in research.

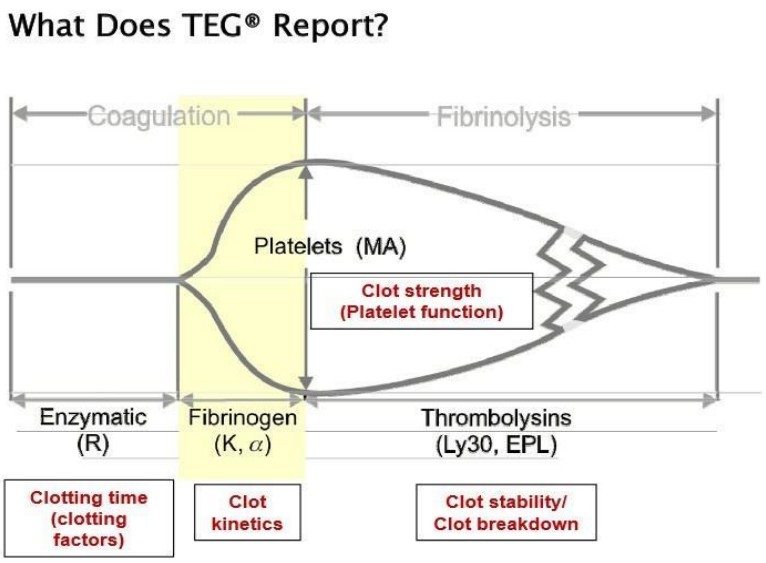


Figure 1. Normal TEG tracing. (Maryland Critical Care Project, n.d.).

TEG provides information on both the coagulation and the fibrinolysis timeline, as seen in Figure 1. Whole blood is placed in the analyzer and activated via the intrinsic pathway and heated to 37 degrees. The sample is then rotated to imitate venous blood flow. A stationary pin is placed in the sample, and as a clot is formed on the pin, the analyzer maps the development, strength, and lysis of the clot. Because whole blood is used for TEG, the contributions of fibrin, platelets and clotting factors can be measured. The individual TEG values are described below.

The **R time** is the reaction time and measures initial fibrin (clot) formation. In a normal patient, this is 5 to 10 minutes. In an anticoagulated ECMO patient, you would expect R time to be longer. This is the only value in a TEG profile that would be considered a "normal" abnormal value. A shortened R time might alert you to a hypercoagulable state. This value is similar in concept to an ACT.

The **K value**, or kinetic value, is the time the clot takes to reach a specified strength and is measured on the TEG tracing from the end of the R time and when the tracing reaches 20 mm in height. This value reflects fibrin-platelet mesh formation. A prolonged K value would suggest insufficient fibrinogen function. The K value is derived from about eighty percent fibrinogen and twenty percent platelet activity.

The **angle**, represented as **α** on the TEG tracing, is the angle calculated from the split point to the tangent where the k value is achieved. This is a result of fibrin and platelet aggregation (fibrinogen function). The angle should fall between 45 and 55 degrees. If the angle is less than 45, then there are likely poor function of fibrinogen and factor VIII. If the angle is greater than 45, no intervention is typically done.

Maximum amplitude (MA) represents the maximum strength of the clot. This value is calculated from when the clot is formed and starts to level off to when it reaches its maximum amplitude on the tracing. Normal range is 50-60 mm. This value measures about eighty percent platelets and twenty percent fibrinogen. A high MA represents a prothrombotic state with hyperactivity of platelets. A low MA results from either low platelet function or low fibrinogen levels.

LY30 is determined when clot lysis starts and is measured by the degradation of the clot over 30 minutes once MA is achieved by measuring the decreasing amplitude. Normal values are 0-8%. Lysis a normal part of the clotting and healing process. However, hyperfibrinolysis can occurs, and are classified as primary or secondary. Primary fibrinolysis is rapid clot breakdown resulting in increased levels of fibrinogen degradation products (FDP). Secondary fibrinolysis is the breakdown of a clot in the setting of systemic hypercoagulopathy, resulting in consumption of coagulation factors. It can be caused by a disease process, such as malignancy or infection, medication, or other causes. It is often an early sign of DIC (Fields, n.d.).

A concerning TEG tracing in the ECMO patient is secondary fibrinolysis. Secondary fibrinolysis may represent the first stage of DIC and may present before the patient's symptoms can alert the care team to the disorder. Causes that lead to this pathology include severe sepsis, trauma, liver transplantation, and cardiopulmonary bypass (Fay, 2017). While DIC is a diagnosis confirmed through clinical presentation and laboratory values, secondary fibrinolysis indicates that the patient is at high risk for DIC (Leung, 2017).

Parameter	Normal Value	Clinical Cause	Treatment
High R time	5-10 minutes	Clotting factor deficiency	Decrease anticoagulation, FFP
Low R time	5-10 minutes	Enzyme hypercoagulopathy	Enzymatic inhibition (Heparin or Bivalirudin)
High K or α-angle	1-3 minutes (K)	Decreased fibrinogen function	Cryoprecipitate
Low K or α-angle	53-72 degrees (α)	Platelet hypercoagulopathy	No treatment
High MA	50-70 mm	Platelet hypercoagulopathy	Platelet inhibition (Plavix)
Low MA	50-70 mm	Decreased platelet function	Platelet transfusion, Ddavp
Elevated LY30	0-8%	Primary fibrinolysis	Consider anti-fibrinolytics
Low R, Low K, High MA, High LY30		Secondary fibrinolysis	Treat cause Consider increasing heparin or antithrombin III
Unexplained bleeding	Normal values	Dysfunctional Platelets Mechanical Bleed	Platelet mapping Consider Ddavp Consider Surgery/OR

Table 1. TEG parameters and interventions.

Implications for Practice

A typical TEG tracing for an ECMO patient is similar to how a hemorrhagic tracing would appear (see Figure 2), with an extended R time. It appears this way as the anticoagulation is doing its job to slow down initial clotting rates. Heparin is a common anticoagulant and when running a TEG, it is important to run one with and without heparinase. The heparinase corrects the tracing by counteracting the heparin and as a result, other coagulopathies that would have been disguised by the heparin are visualized.

At BUMCP, the anticoagulation protocol usually consists of daily TEG with either an aPTT every 2-4 hours, or an ACT hourly. In the case where a patient would have an R time beyond the goal, but the aPTT or ACT is within range, the provider will likely decrease the goal of the aPTT or ACT to help bring the R time down to reach goal. A general range of goal R time in the ECMO patients is two-three times that baseline R time before anticoagulation was started. This range is typically 15-25 but can vary from patient to patient.

In the case of a patient that is bleeding, but has a normal TEG tracing, there are options to explore further or treat. This can include desmopressin, mechanical intervention (i.e. surgery), or platelet mapping, which will be discussed further later on. Desmopressin helps increase the activity of platelets by increasing levels of clotting factors in the plasma, specifically von Willebrand factor, factor VIII, and increases the ability of the platelets to adhere and form clots (Desborough et al., 2016).

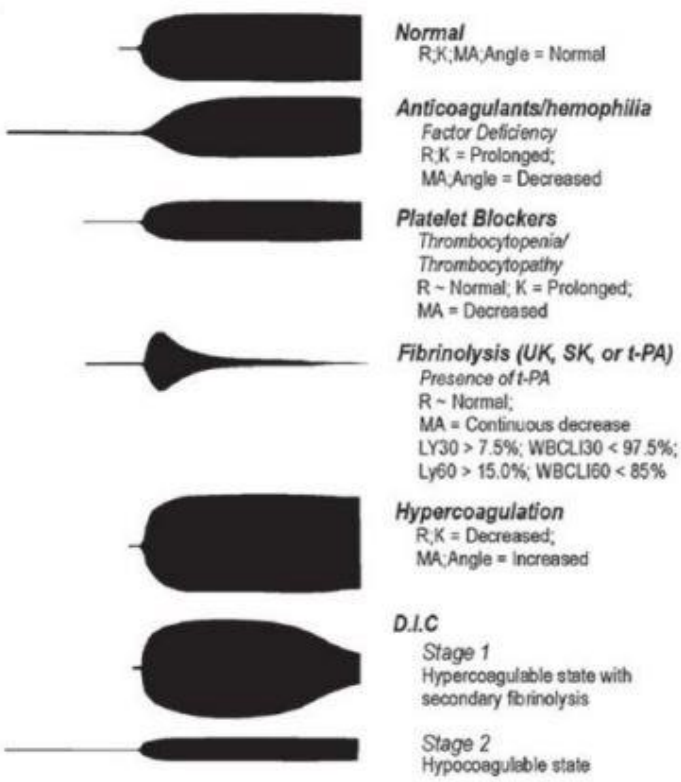


Figure 2. Abnormal tracings (source unknown).

Platelet mapping is an additional test that can be done through TEG. To better understand this, platelet mapping can be done to determine how effective the platelets are to forming clots or not able to (inhibited). Platelet dysfunction can cause unexplained bleeding with a normal or low platelet counts. This dysfunction can be genetic or acquired, caused by drugs or disorders. Typically, in the ECMO patient platelet dysfunction will be due to their underlying disease process and/or interaction with the bypass circuit itself (Kuter, 2019). Drugs that can also affect platelet function are NSAIDs, aspirin, adenosine diphosphate (ADP) receptor inhibitors (such as Plavix or Brilinta) and nutraceuticals. Disease processes that cause platelet dysfunction include systemic lupus erythematosus, myeloma, uremia, and cirrhosis (Kuter, 2019). When in the ECMO circuit, the platelet surface can lose glycoprotein lb/IX binding site for von Willebrand factor through absorption of the circuit surface, and then fibrinolysis may be activated (Kuter, 2019).

Platelet mapping identifies platelet dysfunction by mapping three different tracings, each one respectively represents the maximum amplitude (MA) of the active platelets, inhibited platelets, and maximum platelet contribution (Dickerson, n.d.). Maximum platelet function is when none of the platelets are inhibited and is activated by thrombin in blood sample ($MA_{thrombin}$). In a second channel, a TEG is run with an activator with fibrin, which shows the platelets completely

inhibited (MA_A). A third and fourth channel are run with an agonist, either arachidonic acid (AA) or adenosine diphosphate (ADP), which will show the current activation of the platelets (MA_{AA} and MA_{ADP} respectively). In a patient on ECMO or another mechanical circulatory device, and is on heparin or bivalirudin, the MA_{ADP} is more often compared (Dickerson, n.d.). Patients that are on antiplatelet medication would show more of a response with a MA_{AA}. The ECMO specialist can see the percentage of inhibition shown by the difference between $MA_{thrombin}$ and MA_{ADP}/MA_{AA}.

The current software for platelet mapping requires the ECMO specialist to pick each tracing in a specific order to create an image to compare the multiple MAs. To do this, after ordering platelet mapping, in the software program the ECMO specialist will chose the $MA_{thrombin}$ first, then then MA_A, and then the channel run with the agonist of choice.

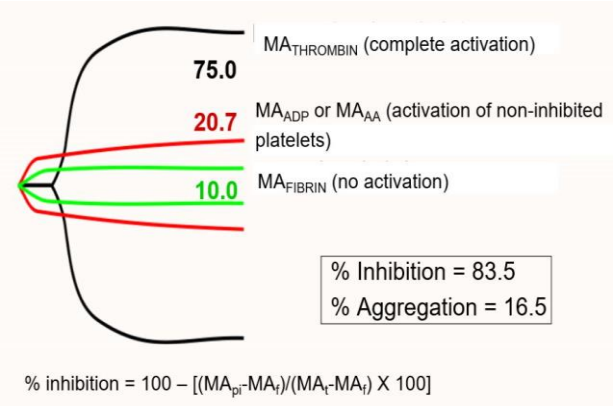


Figure 3. PlateletMapping tracing example (Fields, n.d.).

Summary

As a whole blood test, TEG can provide additional information about the coagulopathy of the ECMO patient. Because coagulation can be greatly skewed in ECMO patients, a TEG provides information beyond what an aPTT and ACT can provide, such as discern between bleeding issues related to low fibrinogen or low platelets. A TEG tracing can also alert the care team when the patient may be entering more dangerous coagulopathies that an aPTT and ACT will not identify, such as DIC and platelet dysfunction. This additional information provided by TEG and platelet mapping can help guide more appropriate treatment for this patient population. Another benefit is to prevent inappropriate blood product transfusions, such as platelets or plasma, which increases the risk of transfusion acquired inflammatory injuries. As practices regarding anticoagulation in ECMO patients advance, the role of the ECMO specialist will be vital in contributing to improving the management and care for these patients. Every hospital will have their specific protocols on anticoagulation, but this module provides a guide to general application and concepts regarding TEG in the ECMO patient for the ECMO specialist.

Post Test

Question 1- What abnormal TEG value do you expect to find in an ECMO patient that is anticoagulated appropriately and has no other pathology?

A. Elevated MA
B. High R time
C. LY30 <8%
D. Elevated K

Answer: B. The goal of anticoagulation in an ECMO patient is to prevent clotting in the circulatory system, including the foreign surface of the ECMO circuit. By increasing the R time, the time to clot is increased, decreasing unwanted clotting in the circuit.

Question 2- In secondary fibrinolysis, what disorder are you concerned the ECMO patient could be developing?

A. Thrombocytopenia
B. Thrombosis
C. Disseminated intravascular coagulopathy
D. Anemia

Answer: C. Secondary fibrinolysis on a TEG can show that inappropriate clot lysis is happening in the patient's circulatory system and can alert the healthcare team that that patient is entering a dangerous coagulopathy (DIC) before they become symptomatic.

Question 3- Your ECMO patient is bleeding copiously from the cannula and central line sites. Their TEG is normal, PTT is within ordered parameters, and platelets are 105,000. What further TEG testing could you order?

A. Fibrinogen level
B. D dimer
C. CBC in 2 hours
D. Platelet mapping

Answer: D. Platelet mapping can help determine if bleeding can be related to dysfunctional platelet, particularly when bleeding exceeds the expectations of other laboratory values.

Question 4- What treatments would be considered in a patient that was in secondary fibrinolysis and is actively bleeding from the cannulation site? (Select all that apply).

A. Increase the anticoagulation medication dose
B. Hold all anticoagulation and call the physician
C. Treat the underlying cause
D. Administer fresh frozen plasma (FFP) and platelets per protocol

Answer: A & C. By increasing the anticoagulation, it can restore anticoagulation pathways and decrease hypercoagulability and consumption of clotting factors. Always treat the underlying cause.

Question 5- What coagulopathy factor(s) contribute to the MA?

A. Von Willebrand factor
B. Platelets and fibrinogen
C. Fibrin
D. Factor V

Answer: B. The MA values is derived from 80% platelet function and 20% fibrinogen function.

Question 6- What signs or symptoms might you expect to see on a TEG with heparinase with an R time of 48, K value of 3.5, and MA of 38?

A. Increased bleeding around the cannula site and other incision areas
B. Fibrin forming in the circuit
C. Increased blood pressure
D. Chatter in the circuit

Answer: A. An R time of 48 is too high for the recommended goal in an ECMO patient and the anticoagulation dose may be too high. A K value of 3.5 could possibly indicate decreased fibrinogen function, and a low MA of 38 could indicate that platelet function may be low as well. Treatment for the K value and MA would not be necessary. The R time is the main concern in this scenario.

Question 7- Overnight the patient had increased bleeding around their cannula site, tracheostomy site, and has required red blood cell transfusions. This morning your patient's R time has gone to 28, from 14 yesterday. Your latest aPTT was 75 from 2 hours ago and your goal aPTT is 60-80. What interventions could you expect to occur?

A. Decrease your heparin rate and recheck a TEG
B. Pause the heparin drip for one hour and check another aPTT
C. Decrease your goal aPTT range to 50-60
D. Give a pack of cryoprecipitate

Answer: C. The patient's R time has had a large increase, as well as increased bleeding to the point of requiring a transfusion. While the patient's aPTT is within goal range, their R time is increasing out of the goal range. This patient may need a lower aPTT goal to keep the R time therapeutic.

Question 8- When you are running a platelet mapping, what tracings do you select in order to compare?

A. $MA_{thrombin}$, MA_{A}, MA_{AA}
B. $MA_{AA,}$ MA_{ADP}, MA_{A}
C. MA_{A}, $MA_{thrombin}$, MA_{ADP}/MA_{AA}
D. $MA_{thrombin}$, MA_{A}, MA_{AA}

Answer: C. This is the correct order to program the current platelet mapping system when a platelet mapping is ordered to compare the different tracings.

Question 9- What is the ideal R time for an ECMO patient?

A. 5-10 minutes
B. 25-35 minutes
C. 20-28 minutes
D. 15-25 minutes

Answer: D. While some hospital policies may differ on this, the goal R time would be 2-3 times the patient's baseline R time. A normal R time is 5-10 minutes, it is estimated a goal R time in an ECMO patient on anticoagulation would be 15-25.

Question 10- In an ECMO patient, what might be a key factor in the formation of clot formation and hemostatic changes? (Select all that apply).

A. Endothelial wall damage
B. Low doses of anticoagulation medications
C. Exposure of blood to the inner surface of the ECMO circuit
D. Anaerobic metabolism

Answer: All of the above. Endothelial wall damage activates several clotting factors, which triggers the clotting cascade. In an ECMO patient, anticoagulation that is at too low of a dose to decrease time to clot formation is not effective and the dose will need to be increased. Exposure to the inner surface of the ECMO circuit is identified by clotting factors as a foreign surface and will activate the clotting cascade as an inflammatory response, similar to endothelial wall damage. Anaerobic metabolism can a

Question 11- TEG is a whole blood test that can measure what in the coagulopathy of an ECMO patient? (Select all that apply).

A. Fibrinogen
B. Platelet function
C. Enzymatic factors
D. Fibrinolysis
E. Time to initial fibrin formation

Answer: All of the above. Fibrinogen function is identified in K value or α-angle. The MA is dependent on platelet count/function. Enzymatic factors are key in the R time value. Fibrinolysis is shown in LY30. Time to initial fibrin (clot) formation is shown in the R time value.

Question 12- What TEG value might tell you that there is decreased fibrinogen function?

A. Prolonged K value
B. Prolonged R time
C. High MA
D. High α-angle

Answer: A. The K value is derived from 80% of fibrinogen function and 20% of platelet function. When the K value is prolonged, there is decreased fibrinogen function, decreasing the time is takes for the clot to reach 20 mm on the TEG tracing.

APPENDIX F:

THE UNIVERSITY OF ARIZONA INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL LETTER

THE UNIVERSITY OF ARIZONA
Research, Discovery & Innovation

Human Subjects Protection Program

1618 E. Helen St.
P.O.Box 245137
Tucson, AZ 85724-5137
Tel: (520) 626-6721
http://rgw.arizona.edu/compliance/home

Date:	March 01, 2019
Principal Investigator:	Amy Lee Moore
Protocol Number:	1902379486
Protocol Title:	Education for Providers on Thromboelastography to Inform Anticoagulation Therapy in Extracorporeal Membrane Oxygenation
Determination:	Human Subjects Review not Required

Documents Reviewed Concurrently:

HSPP Forms/Correspondence: *Moore UA IRB determination of human research_Oct 9.pdf*

Regulatory Determinations/Comments:

- Not Research as defined by 45 CFR 46.102(l): As presented, the activities described above do not meet the definition of research cited in the regulations issued by U.S. Department of Health and Human Services which state that "Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research."

The project listed above does not require oversight by the University of Arizona.

If the nature of the project changes, submit a new determination form to the Human Subjects Protection Program (HSPP) for reassessment. Changes include addition of research with children, specimen collection, participant observation, prospective collection of data when the study was previously retrospective in nature, and broadening the scope or nature of the study activity. Please contact the HSPP to consult on whether the proposed changes need further review.

The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).

Amy Lee Moore <amymoore@email.arizona.edu> Mar 21, 2019, 12:36 PM

to elisebowler, Jessica, Leslie

Hi Jessica,
I had a slight change to my project, and I wanted to verify it would not effect my IRB approval. The same materials that were submitted will be used, the concept of experts reviewing my education module is the same, but instead of a group meeting to review my education module, it will be reviewed individually by each expert. I just wanted to verify that this would still fall under 'not human research' and I can continue. The chair of my committee has approved this change.

Thank you,

•••

Winters, Jessica - (jwinters1) Mar 21, 2019, 1:08 PM

to me, Elise, Leslie

Hi,

You received a determination that this is not considered research as defined by the federal regulations. Your study was considered not generalizable and as long as that's not changing, you still fall within guidelines of not being considered research.

Please let me know if you have any questions.

Thank you,

Jessica Winters, BA
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